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Loma Linda University Center for Christian Bioethics

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Update

Volume 17, Number 2 (November 2001)

Too risky for research?

Human research with vulnerable persons

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The University of California, Los Angeles (UCLA), School of Nursing Center for Vulnerable Populations Research was established at UCLA in 1999. It has been funded by the National Institute of Nursing Research during the last five years as an interdisciplinary center. Immunologists are involved, as well as a biological researcher, behavioral researcher, and a number of professionals in public health. As our boundaries extend, we are offering a number of programs in different, community and university settings. At UCLA, we hold a monthly colloquium, including training workshops and consultation to faculty and students. For nursing there is an ongoing pre- and post-doctoral trainingship in vulnerable populations. A variety of field experiences are offered for pre- and post-doctoral students. We also have an annual research conference, which will be held in April of 2002 in Palm Springs. One of our more recent activities is becoming involved with HIV vaccine preparedness.

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Why did Jesse die?

James Walters, PhD
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The death of Jesse Gellsinger startled America a couple of years ago. It woke up a slumbering bureaucracy in Washington. It made conscientious researchers reevaluate their practices and procedures. Jesse was an 18-year-old with a rare but non-fatal liver disorder. It was being treated successfully. Two years ago at the University of Pennsylvania he was injected with a virus. He quickly developed a fever of 104 degrees, went into a coma, and in a day or two he was dead.

Why did Jesse die? How could such a thing happen at the University of Pennsylvania and particularly at its well-renowned institute for human gene therapy? Yes, the procedures were approved, but in a questionable manner. They went through the local institutional review board, and were to have gone on to Washington for FDA approval, but Washington had been sending mixed signals to researchers about how strict their oversight was. In the last few years, billions of dollars from private industry and pharmaceutical companies were infused into American research. In the process, Jesse became the first victim of gene therapy research.

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Four aims of the center

The major aim of the center is to advance knowledge about health-related problems of vulnerable populations, by supporting ongoing research and new pilot feasibility studies designed to improve health status outreach for vulnerable populations. Each year we fund a minimum of three studies. These pilot feasibility studies are aimed at helping UCLA faculty develop research programs. Our budget from the government includes money that is designated just for this purpose.

Another aim of the center is to strengthen the resources for and the utilization of molecular, cellular, and physiologic assays in studies of the risk and health status of vulnerable populations. We have correlated in a biolaboratory core that provides consultation to people who may be doing some behavioral research and are interested in biomarkers to be used in their research with vulnerable populations. We do the opposite by helping researchers learn some of the behavioral approaches as well. We also have the capacity to do some assays in our laboratory and give priority to our pilot studies in terms of usage of resources.

A third aim is to enhance research support, particularly the development of supportive community networks in all phases of research with vulnerable populations. For example, we help connect a researcher with a community that might become involved in any phase of the research. We are very committed to involving the communities from the very beginning phases. They actually help plan and design the research so that they are partners. We don't go into a community, complete a study, leave, and give nothing back.

A final role is to create mechanisms for interdisciplinary collaborations of scientists in both biological and behavioral research. We bring together people who tend to use qualitative methods with those who use quantitative methods.

Two special projects

We have two special projects. One is a Latino health demonstration project, and the other is a collaborative effort with the Los Angeles County Health Department. The Latino health demonstration project involves participatory research. The method implemented for this project involves the community from the very beginning, including asking research questions, evaluating what questions are appropriate for the studies, and disseminating the results of the study back to the community. We've used this technique with Venice Family Clinic in designing a collaborative study, which now is under review for funding. It relates to culturally competent diabetes education. We attempt to show that nurses from the same Latino background who use certain culturally appropriate strategies have very effective outcomes with these poor and often homeless Latino diabetic patients.

The second project with the Los Angeles County Health Department involves training lay health advisors, who are community outreach workers, to do general health promotion through their churches and schools. This is a project where community members use their own social networks to help improve the health of the people they know.

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HIV vaccine preparedness

As we all know, the HIV/AIDS epidemic continues. Anti-retral-viral drugs and the protease inhibitors are not going to curb HIV worldwide and normal HIV transmission will not be stopped by behavioral interventions alone. There is an increasing interest in an HIV vaccine. We want to know how to get involved with HIV vaccine preparedness. Some of the core leaders of our center have been involved in doing HIV risk reduction studies for some time. We have had very favorable outcomes from our studies. Our interventions have resulted in some improved and less risky behaviors. Overall the results of these studies on an individual basis have been positive, but we want to do more. Behavioral interventions alone are not going to solve the HIV

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epidemic, particularly from a global perspective. We became interested in vaccines as another approach that needs to be taken simultaneously. When we began to explore what was happening in vaccine research, we soon realized that as researchers were moving ahead with vaccine preparation in terms of biologic ends, the personal and behavioral ends, were not being addressed. When we use the term "HIV preparedness," we intend to focus attention upon the issues, both ethical and social, that participants in these trials might have. Fifty-three million people have been infected with HIV worldwide, 19 million have already died, more than 13 million children have been orphaned, and there are 16,000 new cases every day. Ninety-five percent of these cases are occurring in developing countries. It is a global problem that we all have to address and be concerned about.

We decided to hold a vaccine preparedness think tank on August 29, 2001. We pulled together an interdisciplinary group, which included researchers from UCLA, community representatives, people from the county health department, and some pre- and post-doctoral fellows. It was purposely designed to be interdisciplinary and to involve the community so that this would be a beginning phase for strategic planning in terms of HIV preparedness.

Behavioral interventions alone are not going to solve the HIV epidemic...

Vaccine trials have been going on for some time. However, it is often said that ethics and social policy lag behind advances in medical technology. We are trying to address this ethical area related to HIV vaccine preparedness so as not to lag behind.

Awareness of this tragic study is widespread in the community and particularly among vulnerable populations and directly impacts how people respond to us. Going out to the areas where we do our research in east Los Angeles, and saying that we are from UCLA is not necessarily a big plus. Tuskegee is one of the most dramatic examples to keep in mind when you work with people in developing trust.

Three types of trials

We have three types of trials; phase one, phase two, and phase three. UCLA is recruiting participants for a number of trials. Phase one trials focus on low risk participants and a smaller sample to test the safety of vaccines. Phase two trials are conducted with medium to low risk participants and have a larger group of participants. Phase three are efficacy trials, with moderate to high risk patients involving several thousand people. In order to get FDA approval of the vaccine we have to have the vaccines go through these three phases to show that they are safe. Currently, we have more than 10,000 people who have been through the various trials. One large ongoing trial is a phase three, involving more than 5,000 people.

Two types of vaccines

Two types of vaccines are being tested: preventive vaccines and therapeutic vaccines. Preventive vaccines are those given to people who are not infected. They either try to block the HIV from being transmitted or prevent the organism from developing into the disease. Therapeutic vaccines of HIV infected individuals to boost the immune system so they can come back from the disease and do better.

Vulnerable populations and how we define them

We see vulnerable populations as social groups that have an increased susceptibility or higher than the national risk for health related problems. While there are numerous groups that represent vulnerable populations, we are focusing on people of color and low-income people. We also recognize women and children as vulnerable for populations. Homeless persons, persons exposed to hazardous conditions and polluted environments, such as some migrant farm workers, are vulnerable also.

Social concerns of trial participants

As clinical trials are underway, we feel a pressing need to take a closer look at the ethical and social concerns of trial participants and their communities. We know that many people would be very interested in vaccines if the social and political climates were right and the vaccine was highly effective. Hopefully, under those conditions, we wouldn't have to do very much community preparedness. Because this is unlikely in the near future, empirical, focused, cooperative attention by both scientists and the community at risk is needed.

From several qualitative studies we know that there are a number of benefits from participating in a trial. There is a CDC funded study called Project LINKS that connects scientists and communities. This project surveyed African-Americans from Durham, South Carolina, injection drug users from Philadelphia, and gay men and women from San Francisco. Participants spoke positively of the trial. Injection

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drug users especially felt they faced risks every day.

However, we must comment on the parallel concerns and issues raised. There are a number of risks and concerns regarding vaccines themselves. These include negative side effects, the unknown safety of these vaccines, development of HIV antibodies, the risk of contracting HIV/AIDS if an attenuated virus were to be given, restrictions of travel, inability to join the Peace Corps, inability to donate blood or organs, inability to receive future vaccines determined to be most efficacious, and discrimination. For example, injection drug users also said that their street buddies were more comfortable with and had more faith in the street drugs than they did in the government.

We heard from injection drug users and gay men and women how they felt the government had done nothing for more than ten years, and that they believe their population was actually targeted. They felt the government placed little or no value on them as a population group. We would concur that minority communities have been victimized by the government, vis-a-vis research abuse, government neglect, and social discrimination.

Many African-Americans actually believe that the HIV/AIDS epidemic is a biological experiment that has gone wrong. People from minority communities tend to ask us, "Is there a reason they are targeting high risk individuals? Is it perhaps because we're less sophisticated? Is it because we don't ask the difficult questions?"

People from minority communities tend to ask us, 'Is there a reason they are targeting high risk individuals?'

The social consequences of participation include the impact of these vaccines on family, friends, life partners, insurance, and employment. Individuals asked to participate in a vaccine trial have told us that they would increase their risky behavior because of a sense of protection from the vaccine, even though they have no knowledge of the efficacy of the vaccine. Often when somebody receives the vaccine they will then test sero-positive. Many people, particularly Latinos, feel that there may be a direct connection between the CDC and the IRS in terms of outcomes.

Impact on ethical principles

One must also consider the ethical principles relevant to vaccine trials, for example the principle of autonomy or the right to self-determination. Is it possible for a participant to truly get informed consent if the recommended procedures have not been properly evaluated or if they are not aware of the extent of medical uncertainty? Often people will ask us, "Are they going to be honest with us? I want to know when you know what's going on. I don't want no secrets."

There is also the principle of beneficence. Is it unethical to use powerful therapeutic procedures, such as an HIV vaccine, without sound assessment of efficacy and safety? Finally, there is the principle of distributive justice. This is the fair sharing in society of both the benefits and burdens of being part of an investigation.

In underdeveloped countries, the vaccine may never become available. There may not be financial means within the country to provide the benefits of participating. But many of these countries are already participating in the burden, because they are involved in the vaccine trials right now.

In addition to ethical concerns we want to raise again the issues of trust and confidentiality, as well as the consent process. There are some consent processes for vaccine trials that are more than thirty-two pages long and we wonder about the levels of comprehension possible with many of our vulnerable populations. There needs to be some mechanism in place for example, to confirm that they truly understand what they are reading about based on the literature. There is an inverse relationship in terms of the education of the person and their willingness to participate. We wonder if this disparity is because of inability to understand the consent forms.

Community participation

Many community members are appalled by the fact that researchers go to them after the money comes in on research grants and say, "We need to recruit minorities or people of color because we want to make our numbers look right." They want to make sure that when we develop grant funded research projects, we talk about the grant at the same time, and that we talk to people who know the community. We want to involve political people and social leaders at the grass roots level of the community, and seek communication on a level well understood by everyone.

In order that vaccine trials will be conducted ethically and that community participation will become a reality, scientists must walk in the shoes of the participants. They must walk slowly ask a lot of questions. Biological and behavioral researchers need to work together to assure that these qualitative issues are addressed before we urge people to sign up. Community advisory boards are critical so we have people from

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the community directing the researchers and scientists in terms of what's working and what's not. We seek continuous community input and assessment of risks and benefits.

So who is the ideal participant? The ideal participant is someone who understands and asks the right questions, knows what the risks are and understands the procedures and rights that he or she has and knows that there is often no benefit from participating in the beginning phases of the vaccine trials. We recommend educating and including communities in all planning and implementation stages. Providing comprehensive but understandable informed consent, collaboration with local organizations and community members who know the community and it's values is essential.

If you are interested in learning about the educational activities at UCLA, please contact the center to be placed on their mailing list.

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Website: *www.nursing.ucla.edu/son*

Why did Jesse die?...
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Washington's influence

What influence has this had on Washington's review of what is going on in very innovative ways in universities? In 1992 the government was funding half of the research being done in basic science, particularly biomedical science. Today it is being funded at 70% by private pharmaceutical companies in biomedical research. That is a significant issue. There were conflict of interest concerns at the University of Pennsylvania. A particular pharmaceutical firm provided millions of dollars to keep the institute in the black financially. Later it was reported that the institute director had more than $10,000 of stock in this particular firm. If that wasn't bad enough the institute itself also had millions of dollars worth of stock. We will be more successful as we give attention to these sorts of conflict of interest and oversight issues. Research in our universities in the biomedical area will be more adequate than it was in the late 80's as increased pressure came from private firms to speed up trials to get the desired results.

The real issue

We will continue to struggle with a conflict between two significant ethical principles, regardless of cleaning up these sorts of difficulties. Right along with patient autonomy is societal wellbeing. How can we make our society better? That is the sort of thing being done in regard to not just research regarding HIV, but particularly human gene therapy, which has great potential. In recent scientific literature I have read that it is possible for more than a hundred million Americans (two out of five persons) to benefit from breakthroughs that could come through gene therapy. These are people who are afflicted with Parkinson's, Alzheimer's, diabetes, and various heart related conditions. The real issue is whether we can have those benefits while at the same time protecting the Jesse Gellsingers of our country.

I don't think we never sacrifice some individual lives for societal well-being. Take our war on the Taliban even as we speak. Our government leaders acknowledge that there will be some American soldiers who will die. They will die so that many more Americans might live, unlike what happened on September 11th. In biomedical research on human subjects many are convinced that we can proceed without the sacrifice of individual patients. We think that we can have our cake and eat it to. I think that is the big issue. Can we continue our war on disease without having to sacrifice or run roughshod over the sorts of protocols having to do with truly informing and supporting individual subjects in our research?

I particularly applaud the sensitivity to the humans who are participants in research taking place at the UCLA Center for Vulnerable Populations Research. The advocacy of full disclosure of risks, media involvement, community involvement from the very earliest stages, sensitivity to the possibility of exploitation of the poor and the uneducated and various vulnerable populations so that we all might benefit are most laudable.

There are a couple of specifics that I might mention for particular attention. I think about the sophisticated research we do in our leading research universities and teaching hospitals. What safeguards do we take to see that it's only a reasonable risk that we ask various populations, particularly vulnerable populations, to be a part of? When a person is particularly ill, we grasp at whatever might be available. If the researchers haven't done adequate work to make sure that good animal testing has been done and other adequate testing precedes the offering of it to these populations, regardless of all the disclaimers we can give, isn't it likely that many will accept in a rather gullible manner? I wonder if we should give payment to participants in a research protocol. Is the payment just for inconvenience? At what point does payment become an inap-

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propriate inducement to be a part of the study?

Ethically concerned researchers

Let me point to a couple of illustrations that to show how ethically concerned researchers have bent over backwards to protect subjects' rights, I think of Barney Clark in 1982. He was the dentist at the University of Utah's teaching hospital who was the recipient of the first artificial heart. I was impressed that his team was so concerned that he not be overwhelmed by the enthusiasm of the researchers that they assigned him a physician who was not involved with the project as his patient advocate. This physician helped him think through other sides of whether he should enter this experimental program.

Art Caplan served on the IRB at the Hennipen County teaching hospital in the Twin Cities several years ago. He was so concerned about informed consent and a particular protocol that he convinced the other IRB members to assign him to try to talk the potential participants out of doing it. He talked until he was blue in the face, but didn't change one mind. At least he gave the other side.

Literally hundreds of millions of people worldwide may soon benefit from biomedical research protocols. The question is whether this war on disease needs to involve the sacrifice or compromising of patients like Jesse Gellsinger. How we conduct our research will show how we answer that question.

Center for Christian Bioethics
News & events

OCTOBER, 2001

Bioethics Grand Rounds

October 10, 2001—The first Bioethics Grand Rounds featured Deborah Koniak-Griffin, PhD, and Adeline Nyamathi, PhD, from the Center for Vulnerable Populations Research, School of Nursing, University of California, Los Angeles. Their presentation is the basis of the first article in this copy of **Update** regarding ethical issues of research projects they are responsible for. There was a record attendance of more than 180 Loma Linda University students and faculty, Loma Linda University Medical Center physicians, and other local professionals.

NOVEMBER, 2001

New MA program

November, 2001—The Faculty of Religion now offers a master's of arts degree in religion and the sciences. Scholars in these two fields are recently exploring the relation between their respective disciplines. This program invites students with various backgrounds and viewpoints to participate in this dialogue. Loma Linda University affirms the importance of scientific knowledge within the overarching perspective of Christian faith. Currently, students may matriculate upon acceptance into the program.

Contributor's Convocation

November 10, 2001—The Center for Christian Bioethics hosted it's annual Contributor's Convocation at the Desert Falls Country Club in Palm Springs. Three students in the biomedical and clinical ethics masters program spoke on the effect of ethics pertaining to their field of study. Rachel Mason, MS, addressed ethical issues within psychological studies; Tricia Williams, DDS, spoke on patient autonomy in dental ethics; and Georgina Manning, BSN, shared her personal experience of care ethics in pediatric nursing. Ms. Manning's article will appear in **Update**, 17.3.

Loma Linda University's chancellor Richard H. Hart, MD, PhD, concluded the convocation by speaking on the ethical concerns of fulfilling Loma Linda University's mission "to make man whole."

Bioethics Grand Rounds

November 14, 2001—Once again, another highly attended Grand Rounds session featured Katrina Bramstedt, MA, a graduate of the MA program in biomedical and clinical ethics. Her presentation was titled "Ethical Complexities of Total Artificial Heart Technology." She addressed the ethical issues of constructing total artificial heart studies and the candidates chosen for therapy with consideration of the number awaiting a heart transplant.

DECEMBER, 2001

Annual Fundraising Campaign

December 2001—It is time for the Center for Christian Bioethics annual fundraising campaign. Currently, there is significant progress on the development of a new publication for the Center—a collection of approximately thirty-six essays penned by Jack W. Provonsha, MD, PhD, emeritus professor of philosophy of religion and Christian ethics, and founding director of the Center. For more than 18 years, the Center has served the community with careful thinking about the values held dear in the practice of health care. Donations allow the Center to continue broadening the readership of **Update** and increase the Centers' speaking circuit.

Bioethics Grand Rounds

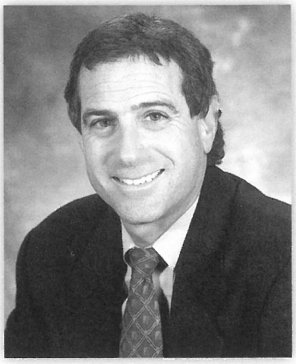
December 12, 2001—The Center for Spiritual Life & Wholeness presented "Transformation After Tragedy: Client Experiences and Clinical Implications." Elizabeth Johnston Taylor, PhD, RN, associate professor, School of Nursing, Loma Linda University, was the speaker. Richard Rice, PhD, professor, Faculty of Religion, LLU; and Claudia Guillaume, clinical specialist, nursing spiritual care and development, Loma Linda University Medical Center, both served as respondents to the presentation. Dr. Johnston focused on how personal perspectives of tragedy affect professional care.

UPCOMING

Bioethics Grand Rounds

January 9, 2002—Gina Jervey Mohr, MD, assistant professor, division of palliative care, department of family medicine, School of Medicine, LLU, will present "Not Dead Yet: The Dilemma Over Dying." Bioethics Grand Rounds are held the second Wednesday of each month in the A-Level Amphitheater, LLUMC from 12:00 noon to 1:00 p.m.

Jack Provonsha Lecture Series presents Ira R. Byock, MD



Established in honor of Jack W. Provonsha, MD, PhD, this lecture series focuses on the integration of ethics, theology, spirituality, and medicine. Dr. Provonsha's pioneering work in Adventist theology and ethics helped shape concepts of wholeness essential in LLU's mission "to make man whole." The lecture is to be held Tuesday, March 12, at 7:00 p.m. at the University Church of Seventh-day Adventists, Loma Linda.

Ira R. Byock, MD, director of The Palliative Care Service, Missoula, Montana, will be the featured speaker. Dr. Byock is also the featured speaker for the annual bioethics conference.

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Watch for brochures.

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